PATENT/Docket No. PC10299A
Appl. No. 09/489,711
Filing Date: January 24, 2000
Office Action Dated: March 16, 2006

REMARKS

I. Preliminary Remarks

In the Office Action, Claims 17, 26-27, 30-32, and 40-41 are pending and under examination. Claims 1-16, 18-25, 28-29, and 33-39 are canceled. Claims 17, 26-27, 30-32, and 40-41 are rejected.

After entry of this paper, Claims 1-16, 18-25, 28-29, and 33-39 are cancelled without prejudice in an effort to favorably advance prosecution of the present application. Applicants reserve the right to pursue the subject matter of the cancelled claims in a continuation application. Claims 17, 26-27, 30-32, and 40-42 are under consideration. Claims 17, 27, 30, and 32 are amended. Claim 42 is new. Support for the amendments to the claims is found throughout the specification. The amendments do not include new matter. Reconsideration and withdrawal of the rejections are solicited for the reasons set out below.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

This Response is timely filed. The USPTO is given authorization to charge Deposit Account No. 21-0718 for any fees necessary with the submission of this Response.

II. Patentability Arguments

A. Rejections Moot.

Applicants acknowledge that the rejections of Claims 13, 16, 24, 25, and 33 are moot (Items 5-10 of the Office Action).

B. Rejections Withdrawn.

Applicants acknowledge that the rejections of Claims 17, 26, 27, 30, 31, 32, and those dependent therefrom are withdrawn in light of Applicants' amendment to the claims and/or the base claims and/or Applicants' arguments (Items 11-17 of the Office Action).

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C. The Rejection of Claim 31 under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn.

Claim 31 was rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and that this is a new matter rejection. Applicants respectfully traverse this rejection.

In response to this rejection Applicants provide the following enumeration of the descriptive support in the specification as filed for the claim limitations of Claim 31.

Support for the antigen composition comprising a fluid fraction of an E. *rhusiopathiae* culture is found at page 2, lines 23-24; page 3, lines 8-12; page 4, line 25 through page 5, line 12; and page 11, lines 21-22.

Support for inactivating the *E. rhusiopathiae* culture with beta-propiolactone is found at page 4, lines 17-19; and page 11, lines 23-25.

Support for a fluid fraction substantially free of cells of *E. rhusiopathiae* is found at page 4, line 34 through page 5, line 3; page 5, lines 13-18; and page 11, lines 21-22.

Support for a stabilizing agent which is a metal hydroxide, a metal phosphate, an aluminum hydroxide gel, a calcium phosphate gel, a zinc hydroxide/calcium hydroxide gel or an alum is found at page 6, line 1 through page 7, line 6; and particularly at page 6, line 29 through page 7, line 17.

Support for a stabilizing agent which is aluminum hydroxide gel and is present at about 30% v/v in said vaccine composition is found at page 7, lines 1-6; and page 12, lines 4-12.

Support for an adjuvant composition comprising about 2% v/v lecithin, about 18% v/v mineral oil, and a combined volume of about 8% v/v of polyoxyethylene sorbitan mono-oleate and sorbitan mono-oleate surfactants is found at page 3, line 34 through page 4, line 4; page 7, lines 21-32; and page 12, lines 18-27.

Support for the composition protecting an animal against *E. rhusiopathiae* infection is found at page 6, lines 1-2; and page 9, lines 11-21.

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Support for a composition which is stable at 2°C to 8°C for at least one year is found at page 6, lines 21-28.

Support for a composition which protects weaned pigs against *E. rhusiopathiae* infection for six months is found at page 9, lines 18-21; and page 9, lines 28-31.

Examples 2, 3, and 4 illustrate that representative embodiments of vaccine compositions of the present invention protected weaned pigs against *E. rhusiopathiae* infection. Example 2 presents a vaccine composition comprising a fluid fraction of an *E. rhusiopathiae* culture from which the bacteria were discarded and which was inactivated with beta-propiolactone, aluminum hydroxide gel (REHYDRAGEL™), No. 1 Adjuvant (comprises about 2% v/v lecithen, about 18% v/v mineral oil, and about 8% v/v surfactant (e.g., about 5.6% v/v Tween 80 and about 2.4% v/v Span 80), with the remaining volume being a saline solution), and protection of pigs against challenge with virulent *E. rhusiopathiae*. Example 3 presents a study in which the vaccine composition comprised the fluid fraction collected from a culture of *E. rhusiopathiae* inactivated with formalin. The fluid fraction was concentrated, and aluminum hydroxide gel was added to the fraction. The concentrate was stored at 4C until vaccine formulation. No. 1 Adjuvant and saline were added to the composition to achieve the final concentration. Piglets were vaccinated at 3 and 6 weeks of age. At 6 months they were challenged with a virulent culture of *E. rhusiopathiae*. Of 20 pigs vaccinated with this vaccine composition, 15 (75%) were completely protected. Example 4 presents a study of a vaccine composition prepared according to Examples 1-3 and held for 12 months. Pigs were vaccinated at about 3 weeks (weaning) and again 3 weeks later. They were challenged with a virulent culture of *E. rhusiopathiae* at about 9 weeks of age. Of 19 pigs challenged, 100% were protected.

The Examiner stated that there is no descriptive support within the instant specification for the vaccine composition claimed in claim 31, which is "required to comprise a fluid fraction of an Erysipelothrix rhusiopathiae culture that is inactivated with beta-propiolactone (BPL) and that is substantially free of cells of Erysipelothrix rhusiopathiae plus a generic 'metal phosphate' or 'metal hydroxide', or 'a calcium phosphate gel', or 'a zinc hydroxide/calcium hydroxide gel or an alum', or 'an aluminum hydroxide gel, and an adjuvant composition comprising about 2% v/v

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lecithin, about 18% v/v mineral oil, and a combined volume of about 8% v/v of Tween 80 and Span 80 surfactants with the remaining volume being saline solution, and is required to be stable at 2°C to 8°C for at least one year, and is required to protect weaned pigs against Erysipelothrix rhusiopathiae infection for six months."

In fact, each and every limitation in Claim 31 is supported in the specification. The CCPA has written "It is not necessary that the application describe the claim limitations exactly... but only so clearly that persons of ordinary skill in the art would recognize from the disclosure that appellants invented processes including those limitations." (See *In re Wertheim*, 541 F.2d 257, 191 USPQ 90, 96 (CCPA 1976)). In addition, the Board explained "Adequate description under the first paragraph of 35 USC 112 does not require literal support for the claimed invention... Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed. (See *Ex parte Parks*, 30 USPQ2d 1234 (BPAI 1994)). As can be seen from the enumeration of the descriptive support in the specification, one skilled in the art would know that Applicants had possession of the concept of what is claimed.

Based on the remarks presented herein, the rejection of Claim 31 under 35 U.S.C. §112, first paragraph, is overcome. Withdrawal of this rejection is respectfully requested.

D. The Indefiniteness Rejections of Claims 17, 26, 27, 30-32, 40, and 41 under 35 U.S.C. §112, Second Paragraph, May Properly Be Withdrawn.

The Examiner rejected Claims 17, 26, 27, 30-32, 40, and 41 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention . Applicants respectfully traverse this rejection.

(a) Examiner states that Claim 32 is vague, indefinite and confusing in the limitation 'Claim 17 or 30, wherein said *E. rhusiopathiae* culture is inactivated with formalin'. Is the *E. rhusiopathiae* culture recited in the dependent claim 32 inactivated for the second time with formalin? Claim 32 has been amended to be in independent format, and a new claim (42) has

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been added to the claim set (see listing of claims above), which renders this rejection moot. Withdrawal of this rejection is therefore respectfully requested.

(b) The Examiner states that Claim 40 is vague, indefinite, incorrect and/or has improper antecedent in the limitation: 'The antigen composition of Claim 17', because claim 17 is drawn to 'A vaccine composition', but not to 'An antigen composition'. Applicants respectfully submit that Claim 17 (1) refers to an antigen composition (see listing of claims above), which is a proper antecedent basis for Claim 40 and renders this rejection moot. Withdrawal of this rejection is therefore respectfully requested.

(c) The Examiner states that Claim 41 is vague, indefinite and incorrect in the limitation: 'The vaccine composition of Claim 40', because as presented currently, claim 40 is drawn to 'The antigen composition' as opposed to --The vaccine composition--. Applicants respectfully submit that Claim 41 depends from Claim 40, which depends from Claim 17. Claim 41 therefore contains all of the elements of Claims 17 and 40. Claim 17 refers to a vaccine composition (see listing of claims above), which is a proper antecedent basis for Claim 41 and renders this rejection moot. Withdrawal of this rejection is therefore respectfully requested.

(d) The Examiner states that Claim 27, as amended, is vague and lacks proper antecedent basis in the limitation: 'the concentrated composition'. Claim 27 depends indirectly from claim 40, which recites 'a concentrated antigen composition'. Examiner suggested that Applicants replace the limitation with --the concentrated antigen composition--. Applicants have amended Claim 27 as suggested (see listing of claims above). Withdrawal of this rejection is therefore respectfully requested.

(e) The Examiner states that Claims 17 and 30 contain the trademark/trade names 'Tween 80' and 'Span 80'..... accordingly, the identification/description is indefinite. Claims 17 and 30 have been amended (see listing of claims above), which renders this rejection moot. Withdrawal of this rejection is therefore respectfully requested.

(f) The Examiner states that Claims 26, 27, 30-32, 40, and 41, which depend from Claim 17 or 30, are also rejected as being indefinite because of indefiniteness or vagueness identified in the base claim. Claims 17 and 30 have been amended as described above (see listing of claims

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above), which renders this rejection moot. Withdrawal of this rejection is therefore respectfully requested.

In summary, for the foregoing reasons, Applicants respectfully submit that the rejection of claims 17, 26, 27, 30-32, 40, and 41for indefiniteness under 35 U.S.C. §112, second paragraph, may be properly withdrawn. Applicants respectfully requests withdrawal of this rejection.

E. The Obviousness Rejection of Claims 17, 26, 27, 30-32, 40 and 41 under 35 U.S.C. §103(a) May Be Properly Withdrawn.

Claims 17, 26, 27, 30-32, 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frantz, *et al.*, (US 5,695,769) in view of Applicants' admitted state of the prior art, Zarkasie, *et al.*, (*J. Vet. Med. Sci.* 58: 87-89, 1996), and Barenholz, *et al.*, (US 6,156,337). Applicants respectfully traverse this rejection.

As stated in the MPEP (§2141), to support an obviousness rejection, four basic criteria must be met. These are (A) The claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) Reasonable expectation of success is the standard with which obviousness is determined. Clearly for prior art to render an invention obvious, it must render obvious the whole invention and not merely some part of the invention (*In re Antonie* 559 F.2d 618, 620, 195 USPQ 6,8 (CCPA 1997)). The prior art must also be considered as a whole including parts that teach away from Applicant's invention. Applicants respectfully submit that these criteria are not met in the Examiner's rejections.

As stated above, for prior art to render an invention obvious, it must render obvious the whole invention and not merely some part of the invention. For example, *in re Papesch* (137 USPQ 43) held:

> From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. The graphic formulae, the chemical nomenclature, the systems of classification and study such as the concepts of homology,

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isomerism, etc., are mere symbols by which compounds can be identified, classified, and compared. But a formula is not a compound and while it may serve in a claim to identify what is being patented, as the metes and bounds of a deed identify a plot of land the thing that is patented is not the formula but the compound identified by it. And the patentability of the thing does not depend on the similarity of its formula to that of another compound but of the similarity of the former compound to the latter. There is no basis in law for ignoring any property in making such a comparison. An assumed similarity based on a comparison of formulae must give way to evidence that the assumption is erroneous.

The argument has been made that patentability is here being asserted only on the basis of one property, the anti-inflammatory activity, and that the compounds claimed and the compound of the prior art presumably have many properties in common. Presumably they do, but presumption is all we have here. The same is true of all of the compounds of the above cases which were held patentable over compounds of the prior art, many of which must have had more in common by way of properties than the compounds here because the relationships, structurally, were even closer than here.

In the present case, the compositions of Frantz do not exhibit the same utility as the compositions of the present invention. A principal feature of the present invention resides in the recognition that antigens in a fluid fraction of an *E. rhusiopathiae* culture can be stabilized by adding a stabilizing agent. Prior to the filing of the present application, the lack of stability of antigens obtained from a fluid fraction of an *E. rhusiopathiae* culture, (i.e., following removal of the bacterial cells) was a serious problem when these antigens were used to formulate a vaccine composition. Thus, the present invention provides a solution to this problem and provides antigenic compositions and vaccines that are effective in providing long-term protection against erysipelas in animals. As claimed in Claims 17, 30, and 32, compositions of the present invention comprises a fluid fraction of an inactivated *E. rhusiopathiae* culture. The vaccines are claimed to include an adjuvant, which comprises about 2% v/v lecithin, about 18% v/v mineral oil, and a combined volume of about 8% v/v of polyoxyethylene sorbitan mono-oleate and sorbitan mono-

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oleate surfactants with the remaining volume being a saline solution. Applicants respectfully submit that Frantz *et al.* do not teach a vaccine composition containing an inactivated *E. rhusiopathiae* fluid fraction with the specific adjuvant as presently claimed, i.e., an adjuvant with the specific amounts of specified ingredients as recited. Applicants respectfully submit that Frantz *et al.* do not describe the inclusion of a surfactant in the vaccine compositions containing *E. rhusiopathiae*, and in particular do not include the surfactants polyoxyethylene sorbitan mono-oleate and sorbitan mono-oleate.

Examiner stated that the aluminum hydroxide in Frantz's composition intrinsically served as a stabilizing agent is implicit from the teachings of Frantz *et al.* in light of what was known in the art. For instance, Barenholz *et al.* taught the dual role of aluminum hydroxide both as an adjuvant and as a stabilizer in microbial vaccines (see column 13, last two lines). However, Barenholz provides conflicting teachings in this matter. Barenholz states that freezing destroys potency and storage above or below recommended temperature may reduce potency. They state that the instability is related to the aluminum hydroxide which serves as the adjuvant (see Column 8, lines 23-29). Thus Barenholz teaches away from using aluminum hydroxide as a stabilizing agent.

Examiner stated that Zarkasie et al. expressly taught that protective antigens of *Erysipelothrix rhusiopathiae* are abundant in the culture filtrate (see page 89, right column), or rich in culture supernatant (see page 90, left column). However, Applicants respectfully submit that Zarkasie et al. teach a composition prepared from a whole broth culture of *E. rhusiopathiae* (i.e., containing both a culture fluid fraction and cells of *E. rhusiopathiae)* and aluminum hydroxide gel. Zarkasie et al. do not teach or suggest making a culture filtrate that is substantially free of cells of *E. rhusiopathiae.* Accordingly, it is respectfully submitted that the antigenic compositions and vaccine compositions, as presently claimed, are not rendered obvious by Zarkasie et al. In addition, Zarkasie, et al. do not disclose an antigen composition that is stable at 2°C to 8°C for at least one year and provides immunity to weaned pigs for at least six months. Therefore, Zarkasie et al. do not teach the antigenic composition, as presently claimed.

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Applicants respectfully submit that none of the references cited by the Examiner suggest Applicants' invention. There is no indication in any of the references that would suggest that the references be combined. Moreover, even when combined the references do not yield Applicants' invention. Thus, based on the remarks presented herein, the rejection of Claims 17, 26, 27, 30-32, 40 and 41 under 35 U.S.C. §103(a) is overcome. Because none of the references, alone or in combination, teaches Applicants' invention, withdrawal of the rejection is respectfully requested.

III. Conclusion.

In view of the amendments and remarks made herein, Applicants respectfully submit that Claims 17, 26-27, 30-32, and 40-42 are in condition for allowance and request expedited notification of same.

Respectfully submitted,

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